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Abstract:

Background: Systemic right ventricle (sRV) dysfunction in d-transposition of the great arteries following atrial switch (d-TGA) is associated with increased mortality. We aimed to characterize maladaptive sRV mechanisms in d-TGA patients, analyzingrelation of echocardiographic parameters of sRV systolic functionto objective measurements of exercise capacity.

Methods: Forty-seven adult patients with d-TGAand atrial switch(mean age 31.6±4.2 years)underwent conventional echocardiography, bidimensional strain (2D-strain), cardiac magnetic resonance (CMR) imaging and cardiopulmonary exercise evaluation on the same day. Those with median peak oxygen uptake (VO2)>64.5% (n=23) constituted group A,those with VO2≤64.5% (n=24) constituted group B and 23 healthy age and gender matched subjects (n=23) constituted the control group.

Results: In group A, global longitudinal peak systolic 2D-strain (GLS) of sRV was significantly reduced compared to GLS of normal RV and LV in the healthy control group ($p< 0.01$), however peak longitudinal 2D strain was similar at basal and mid-segment of sRV free wall than normal LV. In group B, GLS was significantly reduced compared to group A (-10.9±2.9% vs -13.1±2.3%,$p<0.05$), mostly due tosignificant decrease of interventricular septum longitudinal strain. Other echocardiographic systolic parameters were not significantly different between group A and B.Only sRV GLS showed significantcorrelation with functional capacity as measured by VO2 ($r=0.42$, $p<0.01$), while CMR RVEF did not.

Conclusion:GLS of sRV predicts functional capacity and may be more sensitive than CMR RVEFin detecting early myocardial damage of sRV in patients with d-TGA and atrial switch.

Keywords: Transposition of the great arteries;systemicright ventricle; magnetic resonance imaging; strain.

Introduction:

In patients with transposition of the great arteries (d-TGA) with a Mustard or Senning procedure, the morphological right ventricle (RV) serves as the systemic ventricle (sRV).The native trabeculated RV myocardium undergoes extensive trabecular hypertrophy as an adaptive mechanism to enable pumping in the systemic circuit. However over time maladaptation ensues and long-term follow-up of these patients shows that reduced function of the sRV is associated with increased cardiovascular events and mortality[1, 2]. The evaluation of the sRVsystolic function by using conventional ejection fraction indices continues to pose major challenges.

Cardiac magnetic resonance (CMR) is now considered the gold standard for the assessment and follow-up of sRV volumes and ejection fractionin d-TGApatients after atrial switch operation[3]. The complexity of the shape and dynamic physiology of the sRV raise the need for validation of additional echo derived sensitiveparameters to obtain periodic quantitative estimatesof RVfunction. The longitudinal arrangement of the deep RV myocardial fibers from the tricuspid valve annulus to theapex, make the longitudinal shortening of the RV greater than the radial[4]. Therefore, measurement of the RV longitudinal shortening could be a valuable adjunct to estimate sRV systolic function in patients after atrial switch. We hypothesized that sRV longitudinal 2D-strain could bemore sensitive in detecting early myocardial dysfunction comparedtoconventional measuressuch as ejection fractionin this specific population.

Subjective functional assessment of patients with congenital heart disease is often flawed because these patients present themselves as being asymptomatic while objective measurements show strong limitations at exercise. Moreover, correlation between peak oxygen consumption and sRV ejection fraction are controversial[5, 6]. Considering the potential usefulness of 2D-strain in evaluating sRV function in this setting, we planned to correlate 2D-

strain of sRV with exercise capacity, in a population of adult patients after atrial switch for transposition of the great arteries.

Methods:

We conducted a single-center, prospective, case-control study that included patients with d-TGA following atrial switch, and age- and sex-matched healthy volunteers. The study was performed in accordance with the principles set out in the declaration of Helsinki and was approved by the local ERB(Comité de Protection des Personnes, Paris, Ile de France). All patients and healthy volunteers provided written, informed consent to participate in the study.

From February 2011 to March 2012, 49 patients with d-TGA after atrial switch (32±4 years old, 12 women) were studied. Patients with contraindication for CMR, gadolinium injection, and cardiopulmonary exercise test (CPET), patients with residual ventricular septal defect, prosthetic systemic atrioventricular valve, and pregnant women were not included in the study. All eligible patients werefurther divided in 2 groups according to the median percent predicted peak VO2 value, which was found to be 64.5%. Patients with predicted peak VO2 > 64.5% formed the group A, and patients with predicted peak VO2 ≤ 64.5% formed the group B. To characterize adaptive mechanisms of sRV functionwe compared group Ato 23 healthy subjects matched for age and sex (control group), and to determine sensitive echocardiographic parameters of sRV function dysfunction, group A was compared to group B. Group A, with the highest VO2 values, was considered as the patients group with the best adaptive mechanisms of sRV to systemic afterload, and the group B, with the lowest VO2, was considered as the patients group with maladaptive mechanisms of sRV function to systemic afterload. Healthy subjects were recruited at the ClinicalInvestigationCenter of the institution via a press release after d-TGA patient inclusion. Each subject provided their medical history and underwent a complete physical examination and routine laboratory

evaluation, including an electrocardiogram. All patients and healthy subjects had echocardiography, CMR and CPET all within 24 hours.

Transthoracic echocardiography was performed using a GE-VingmedVivid 7 system (Horten, Norway) with high frame rate (60-90 Hz). Echocardiograms were examined by one of the investigator (M.L.), who was blinded to CMR and CPET data. Complete two-dimensional, Doppler color-flow, spectraland Tissue Doppler studies were performed, and tricuspid regurgitation (TR) was graded as mild, moderate,or severe, according to the guideline of the American Society of Echocardiography[7, 8, 9].Systolic RV function indices were measured according to recent American Society of Echocardiography guidelines[8]. Right ventricle fractional area change (FAC) and tricuspid annular plane systolic excursion (TAPSE) were measured in the apical 4-chamber view. Doppler method was used to measuredP/dTas the time required for the systemic auriculo-ventricular valve regurgitation jet to increase velocity from 1 to 3m/s, from the ascending limb of the TR continuous-wave Doppler signal. Velocity time integral (VTI) was measured from pulsed-wave Doppler signal of the right outflow tract. Systolic excursion velocity (S),isovolumic acceleration(IVA) and Tei index[10]were measured using pulsed Doppler Tissue Imaging, with Doppler sample volume placed in the tricuspid annulus of the RV free wall.

Using a dedicated software package designed for LV strain measurement (Echopac PC; GE Healthcare, Waukesha, Wisconsin), 2D strain was measured by using standard bidimensional acquisitions. The RVand the LV, visualized from the apical 4-chamber view, weredivided into 6 segments and each segment was individually analysed. By tracing endocardial contours on end-diastolic frames, the software automatically tracked the contour on subsequent frames.End systole was defined by aortic valve closure. Adequate tracking was verified in real-time and corrected by adjusting the region of interest or by manually correcting the

contour to ensure optimal tracking.Two-dimensional longitudinal and transverse peak systolic strains (i.e. radial strain) were assessed in apical 4 chamberview(Figure 1). Average longitudinal and transverse peak systolic strains were globally calculated for the right and left ventricles, regionally forRV free wall, interventricular septum and lateral left ventricle wall, at basal, mid and apical level. Two-dimensional longitudinal and transverse peak systolic strains were measured on the same consecutive cycles by analysing offline 2D acquisitions.

Measurements were repeated three months apart by the same observer (ML) and by a second blinded observer (AL). Each observerindependently performed the measurements for 13 randomly selected patients,corresponding to 78 segments(78longitudinal and 78 transverse strains). The reader was allowed to select the best cardiac cycle to perform the measure each time.

All CMR examinations were performed on a 1.5 T system(SignaHDx, GEMS, Waukesha, WI, USA)using a dedicated 8-channel phased array surface cardiac coil.For volumetric and functional imaging, breathhold standard cine steady-state free-precession (SSFP)sequences inshort-axis, 4- and 3-chamber views and RV vertical long-axis orientation were acquired.CMR image analysis was performed by aninvestigator (E.M.), using QMASS platform and software (Medis, the Netherlands), resulting in RV end-diastolic (ED) and end-systolic (ES) volumes, and RVEF (%).Measurements were repeated apart by the same observer (EM) and by a second blinded observer (GS) in 23 randomly selected patients.

Each patient had to perform an exercise stress test on a bicycle ergometer (Sensor Medics, Yorba Linda, CA) with measurements of oxygen consumption (VO2). After a 2 min warm-up period the workload was increased by 10–20 Watts/minute (according to the level of fitness) using a ramp protocol until exhaustion.Patients were encouraged to perform maximal exercise. Testing was terminated after the patient reached the target heart rate (based on age) or because of fatigue, dyspnea, leg discomfort, systolic blood pressure >250mmHg, ventricular

tachycardia, or ischemic electrocardiographic changes. Respiratory quotient during exercise testing (target 1.1) was used to indicate whether maximum work had been achieved. Peak oxygen consumption (peak VO2), oxygen pulse (VO2/heart rate), and the minute ventilation-carbon dioxide production relationship (VE/VCO2 slope) were assessed from gas exchange measurements. Maximal exercise and peak circulatory power were assessed to estimate the level of maximal exercise capacity.

Statistical Analysis:

Datawere presented as mean value ± SD when variables were normally distributed, and median value with 95% of confidence interval when they were not. The group A and Bof d-TGA and the control group of healthy subjects were compared by 2-sample t tests or Mann-Whitney when appropriate.Correlations between echocardiographic parameters, CMR RVEF and CPET measurements were tested by Spearman correlation, and adjustments were madeusinga multiple regression. If the r-value<0.4, the correlation wasconsidered weak; 0.4<r<0.5: moderate and if r> 0.5, then the correlation is strong.A 2-tailed p value ≤0.05 was considered to be statistically significant. The repeatability (intraobserver variability) and reproducibility (interobserver variability) of the CMR and echocardiographic parameters were observed by calculating the variability coefficient as the difference between the two observations divided by the means of the observations, expressed as percentage, and analyzed using intraclass correlation coefficients. For the interobserver study, the mean of the two measures by the first observer was used. Alldata were analysed using MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belium; http://www.medcalc.org; 2013).

Results:

Study population

Patient and control characteristics are summarized in Table 1. Two patients were excluded because sRV free wall could not be adequately visualized during standard echocardiography. Of the remaining 47 patients(32±4 years old, range 22-39 years, 12 women), 13 were operated on using Mustard procedure and 34 usingSenning procedure, combined with ventricular septal defect closure in 2 patients, at a median age of 6.6 months of age, 95%CI [3.8 – 12.2]. The average length of time between the initial surgery and the study was 31.4±7 years. Two patients were in junctional rhythm during the study. Only one patient had undergone additional cardiac surgery after the initial operation to treat a pulmonary venous pathway stenosis. Five patients were in NYHA functional class II, one in class III and the remaining in class I. Only 2 patients had moderate to severe tricuspid regurgitation, and one patient had severe pulmonary stenosis.Twenty three d-TGA patients with peak VO2>64.5% formed group A, and 24 with peak VO2 ≤ 64.5% formed group B.No difference in age and sex was found between group A, B and controls. Blood pressure and heart rate were not different between the 3 groups.

Relation between parameters of sRV function and NYHA functional class

There was no significant difference of peak oxygen uptake between patients with NYHA=1 (n=41, predicted peak oxygen uptake=62.3±10.1%) and patients with NYHA>1(n=6, predicted peak oxygen uptake=58.7±10.8%, p=0.2). Among standard echocardiographic parameters of systemic RV function, only peak S wave and IVA were significantly lower in patients with NYHA>1 compared to patients with NYHA=1 (respectively, p=0.02 and p=0.03). Speckle tracking measures were not related to NYHA functional class, exceptGLS of

systemic RV which was significantly lower in patients NYHA>1 (-12.6±2.7% vs -9.5±3.8%, p=0.01). CMR RVEF was also significantly lower in d-TGA patients with NYHA>1 (42±17.8 vs 50.3±8.3%, p=0.03), with RVEF ≤30% in half of these patients.

Echocardiography parameters of sRV function:

Echocardiography and exercise test outcomes of group A and B compared to controls are summarized in Table 2 and 3.

Percent predicted peak oxygen uptake value was significantly lower in group A than in controls (74% vs 96%, p<0.01, table 2). CMR RVEF was similar in d-TGA patients of group A and of healthy subjects (50±8% vs 50±11%, p=0.9), and was lower than CMR LVEF of healthy subjects (59±5%, p<0.01). All standard echocardiography indices of sRVlongitudinal function (IVA, TAPSE, peak S wave and Tei index) weredecreased in d-TGA patients of group A, compared to RV and LV controls. Only outflow tractVTIand dP/dT of systemic ventricle were not different. Longitudinal peak systolic 2D strains of each sRV segment of d-TGA patients in group Awere significantly reducedcompared to corresponding strains estimated in normal RV. Global longitudinal peak systolic 2D strain of sRV was lower than those of normal LV, however peak systolic 2D strain of the basal and mid segments of sRV free wall in d-TGAwere not different than basal and mid segment of LV lateral wallin controls. Global longitudinal peak systolic 2D strain of the pulmonary LV was not different than those of the RV in controls. Globaltransverse peak systolic 2D strain of sRVin group A wasnot different to normal RV, but was significantly reduced compared to normal LV. This reduction mainly touched interventricular septum.Transverse peak systolic 2D strain values of RV free wall were higher in sRV than in normal RV, reaching values of theLV lateral wall from the controls. This increase mainly concerned the basal sRV free wall.

When we compared group A and B, systemic RVEF was not different (group A=50±8% vs group B=45±10%, p=0.5).Patients with lower exercise performance (group B) had a

significant reduction of global peak systolic 2D strain and of septal longitudinal peak systolic 2D strain compared to d-TGA patients of group A. There was no difference in global longitudinal peak systolic 2D strain of the pulmonary LV,global transverse peak systolic 2D strain of sRV and longitudinal strain rate of sRVbetween the 2 groups.

Relation between parameters of sRV function and peak oxygen uptake:

In univariate analysis, only GLS (r=0.42, p<0.01) and basal longitudinal peak systolic 2D strain (r=0.40, p=0.02) correlated moderately with peak oxygen uptake expressed as a percentage of predicted values(table 4, Figure 2). This correlation was not observed in the healthy subjects (r=0.12, p=0.6, Figure 2). None of the volumetric CMR parameters of sRV (indexed ED RV volume, indexed ES RV volume, indexed mass, andRVEF) correlated with exercise capacity, in d-TGA. Furthermore, no association was found between peak oxygen uptake and either tricuspid regurgitation grade, sRV standard echocardiographic parameters, pulmonary LV global longitudinal peak systolic 2D strain orsystemic RV transverse strain derived from speckle imaging parameters (table 4). GLS remained significantly correlated with peak oxygen uptake as percentage of predicted value, after adjusting for systolic BP, age, sex, complexity of d-TGA, and treatment of cardiac failure(r=0.41,p=0,01). Systemic RVEF as well asGLS and GTS were not correlated with anaerobic threshold, oxygen pulse,VE/VCO2 slope and peak circulatory power. No correlation was found between GLS and systemic RVEF.

Reproducibility:

Intra-class correlation coefficient for intra observer and inter observer reproducibility of GLSwere respectively 0.95, 95%CI [0.82-0.98] and 0.93 [0.75-0.98], and the coefficient of variation was 6.7% and 8.6% respectively for GLS.Feasibility of this measurement was 93%.The reproducibility for GTS was lower with: intra-class correlation coefficient for intra

observer=0.73 [0.52-0.86] and inter observer reproducibility=0.65|0.49-0.80], and coefficients of variation were23.1% and 26.4% respectively.

Intra-class correlation coefficient for intra and inter observer reproducibility of CMR sRVEFwere respectively 0.96, 95%CI [0.90-0.98] and 0.94, 95%CI [0.85-0.98], and the coefficient of variation was 2.8%and 3.4%respectively.

Discussion

Global longitudinal peak systolic 2D strain of sRV is the only echocardiographic parameter of sRVsystolic functionwhich is moderately related to peak oxygen uptakein our study. SystolicRVEF decrease is associated with NYHA functional class impairment. However, NYHA functional class underestimates exercise limitations of patients with d-TGA, and systemic RVEF is not related to peak oxygen uptake. GLS seems to be more sensitive for detectingsRV dysfunction than the gold standard, CMR RVEF, which is not predictive of exercise performance.

Echocardiographic parameters of sRV function in patients according functional tolerance:

All standard echocardiographic parameters of longitudinal sRV function (TAPSE, peak S, IVA and longitudinal strain) in the group of d-TGA patients with the highest VO2 are significantly reduced, compared to healthy controls with anatomic LV as systemic ventricle. Like in previous studies, we confirm that there is a significant reduction of longitudinal strainin sRV of d-TGA following atrial switch[11, 12, 13]. A decrease in RV longitudinal strain is well described when afterload increases[14]. Longitudinal RV deformation was mainly impaired by increased RV afterload, because RV myocytes arrangement is predominantly longitudinal, to create a peristaltic contraction from the inlet to outlet and a bellows-like motion of the free

wall toward the septum[15]. From our results, 2adaptive mechanisms of RVchronically and congenitally submitted to systemic afterload may be drawn: 1/ longitudinal strain values at basal and mid segmentsofsRV free wall are preserved in group A compared to basal and mid segments strain values of normal LV at lateral wall;2/ transverse 2D strain valuesat the basal segment of sRV free wall increase compared to values at corresponding segments of normal RV,so that they reachthose of normal LV. This shift in the sRV free wall from longitudinal to transverse deformation was already observed in sRV[11, 12]. It mainly concerns basalsegment ofsRV free wall. We also observe a correlation between longitudinal strain of this segmentand peak oxygen uptake, unlike the other segments of sRV free wall.Inward movement of the RV free wall is very important during early phase of RV contraction, inducing the peristalsis like bellows effect. So, deformation of the basal segment of sRV free wall may be preserved or increased to maintain a normal cardiac output. GLS is decreased in patients with lower VO2 as well as symptomatic patients (NYHA>1), whereas sRVEF is only impaired in patients with NYHA>1, and is no related to VO2. GLS seems to be more sensitive than sRVEF to detect myocardial dysfunction in sRV.

Relations between parameters of sRV function and exercise performance.

A decrease in the functional capacityofd-TGApatients after an atrial switch is above all related to an impairment of longitudinal function with a decrease of TAPSE, peak S wave and longitudinal 2D strain, while RVEF does not change. Interventricular septum longitudinal deformation is moreimpaired than sRV free wall deformationsuggesting the probable role of RV-LV interdependence in exercise limitationof d-TGApatients following atrial switch. RV-LV relationship was also shown in the Diller et al study with a systemic and pulmonary longitudinal 2D strain correlation in patients with TGA[16].

A decrease in systemic RVEF of group B compared to group A is not statistically significant, whereas all longitudinal function parameters (TAPSE, peak S wave and GLS) are reduced in group B compared to group A. The preservation of transverse deformation (GTS) mayexplain the absence of sRVEFdifference between the 2 groups. Previous data on the relation of RVEF at rest and exercise capacity in patients with sRV have been conflicting. Lack of correlation betweenexercise capacity and indices of left ventricular performances at rest in acquired heart failure has been previously reported[17].Here we have shown that longitudinal strain of sRV correlates moderately with peak oxygen uptake, but thatsystemic RVEF does not correlate with exercise parameters. Similarly, Donal etal.[18] have shown that global longitudinal strain of LV correlated better than LVEF with exercise performances in chronic heart failure.As previously described, no correlation was foundbetween GLS and RVEF, meaning that GLS and RVEF do not definitely provide the same information about systemic RV function[19], mainly because RV myofiber arrangement is predominantly longitudinal[15,20].

Limitations: The group A and B were formed by finding the median VO2, a value intrinsic to this specific set of patients, rather than clinically meaningful cut-off as NYHA functional class. This was explained by the limit of subjective functional assessment in patients with congenital heart disease illustrated by patients with low peak oxygen uptake in NYHA 1 (19/24, 79%). We only studied systolic function, but abnormal diastolic function due to restrictive atrial baffles can also restrict a rise in stroke volume at exercise[21]. Transverse strain measured from apical view has got a poor reproducibility.This result could be explained by off-plane radial displacements of sRV tissue in the apical view.Because of the shape of the RV, most of parameters of function could not include the RV outflow tract. The population included here is a selected one for methodology reasons, limiting the number of study patients. However, atrial switch population is likely to contain patients with pacemakers, often with sRVdysfunction[22].

Conclusion

In patients with d-TGAafter atrial switch, longitudinal and transverse deformations are significantly reduced compared to controls, except in basal and mid regions of the systemic ventricular free wall. This adaptive response may allow sRV to support normal cardiac output, even if the systemic RVEF is lower than healthy subjects. Measurement of RV longitudinal 2D strain is better correlated to exercise intolerance thansRVEF which is the gold standard to evaluate sRV function. RV longitudinal 2D strain should be part in evaluation of sRV function.

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Figures legends

Figure 1: Global longitudinal peak systolic 2D strain (panel A), and transverse peak systolic 2D strain (panel B) of sRV in a d-TGA patient from group A on the left, and of normal sub-pulmonary RV in a healthy subject on the right.

Figure 2: Regression curve between peak oxygen uptake and global longitudinal peak systolic 2D strain (GLS) of sRVin d-TGA and LV in controls

Tables:

	Global d-TGA population (n=47)	**group A (n=23)**	**group B (n=24)**	**controls (n=23)**
Age, mean±SD, years	31.6±4.2	33.0 ± 4.9	33.5 ± 6.0	32.6 ± 7.0
Sex ratio (M/F)	12/35	17/6	18/6	17/6
BSA, mean±SD, m^2	1.8±0.2	1.9 ± 0.2	1.8 ± 0.2	1.9 ± 0.2
Systolic BP, mean±SD, mmHg	114.6 ± 12.0	114.7 ± 12.4	114.6 ± 11.8	115.9 ± 7.5
Diastolic BP,mean±SD,mmHg	70.8 ± 11.0	70.1 ± 10.9	71.5 ± 11.2	68.7 ± 6.1
Heart rate, mean±SD, bpm	66.9 ± 11.2	65.8 ± 8.9	66.4 ± 11.8	63.2 ± 10.2
History of heart failure, n (%)	3 (6.2)	1(4)	2 (8)	_
History of arrhythmia, n (%)	10 (21.3)	5 (21.7)	5 (20.8)	_
NYHA I/II/III/IV, n	41/5/1/0	23/0/0/0	19/4/1/0	23/0/0/0
Sinus rythm, n (%)	45 (95.7)	22 (96)	23 (96)	23 (100)
QRS duration, mean±SD, ms	97±25	105±52	97±39	_

Treatment				_
ARA2- ACEinhibitors	5	1	4	
B-blockers	7	4	3	
Diuretics	1	0	1	
CMR				
RVEDV, mean ±SD, ml/m²	93±31	89 ± 12	98 ± 40	85 ±16
RVESV, mean ±SD, ml/m²	50±26	43 ±14	57 ± 34	40 ± 8
RVEF, mean ±SD, %	47±9	50 ± 9	45 ± 10	50±11

Table 1: Demographic, clinical and CMR characteristics in d-TGA (global population, group A and B) and controls. ARA2: angiotensin receptor antagonist 2- ACE inhibitors: antagonist conversion enzymeinhibitors, CMR: cardiac magnetic resonance imaging, RVEDV: right ventricle end-diastolic volume, RVESV: right ventricle end-systolic volume, RVEF: RV ejection fraction. No difference was significant between group A and B.

Variable	Healthy subjects (n=23)	Global d-TGA population (n=47)	Group A (n=23)	Group B (n=24)	p-value
Exercise duration (sec)	666 [601-744]	599 [483-672]	551 [480-660]	486 [412-559]	<0.001
Peak systolic BP (mmHg)	176 [158.5-195]	160 [140-179]	153[140-165]	147 [133-178]	0.02
Peak diastolic BP (mmHg)	86 [78-94]	85 [75-93]	81 [71-93]	83 [75-90]	0.3
Peak heart rate, (bpm)	176 [170-183]	166 [154-176]	166 [157-171]	154 [145-161]	<0.001
Peak VO2 (%)	96[79-106]	74 [63-90]	74 [70-79]	60 [52-62]	<0.001
Peak VO2, L/min	2.6 [2.1-2.8]	1.9 [1.5-2.5]	1.8 [1.4-2.0]	1.6 [1.2-1.9]	<0.001
Anaerobic threshold (%)	52 [45-62]	41 [34-49]	42 [35-46]	32 [29-36]	<0.001
VE/VCO2 slope	27 [26-29]	30 [27-35]	31 [30-36]	35 [31-40]	<0.001

Table 2: Results of exercise test in group A, B and controls. Values are medians [interquartile range].p values were given for the comparison between global d-TGA population and controls. BP: blood pressure

	Systolic parameters	**d-TGA (n=47)**		**Control n=23**	
		group A (n=23) systemic RV	**group B (n=24) systemic RV**	**RV**	**LV**
Standard parameters	FAC, median 95%CI, %	38 [33 – 42]	36.8 [32-39]	61 [51-66]§	_
	dP/dT, median 95%CI, mmHg/s	868 [723-1111]	1220 [723 – 1263]	273 [186-333]§	947 [735-1114]
	outflow tract TVI, median 95%CI, cm	19 [17-23]	18 [15-20]	21±5	21±4
	IVA, median 95%CI, m/s²	0.9 [0.7-1.2]	0.8 [0.7-1.1]	2.0[1.6-2.8]§	3.2 [2.7-3.6]¥
	APSE, mean±SD, mm	12.5 ±2.9	10.3±3.5*	23.2±3.7§	15.3±3.0¥
	Peak S wave, median 95%CI, cm/s	8.0 [7.0-9.0]	6.0 [5.0-7.0]*	13.9±2.2§	12.2±2.5¥
	Tei, mean±SD	0.41±0.12	0.46±0.12	0.40±0.16§	0.26±0.16¥
Speckle tracking parameters	GLS, mean±SD, %	-13.1±2.3	-10.9±2.9*	-19.5[-19.9- -21.1]§	-18.1±2.6 ¥
	Free wall LS, mean±SD, %	-14.6±3.4	-11.7±5.2*	-23.1±9.3§	-17.3±3.6¥
	Basal LS, mean±SD, %	-17.4±6.9	-15.0±7.3	-28.2±10.6§	-19.6±6.5

	Mid LS, mean±SD, %	-15.0±5.6	-12.6±6.9	-25.6±7.9§	-16.9±4.6
	Apical LS, mean±SD, %	-8.8±5.6	-8.8±4.7	-18.9±9.1§	-15.1±6.8¥
	Septum LS, mean±SD, %	-12.1±2.4	-9.2±3.3*	-19.0±3.1§	
	GTS, median 95%CI, %	14.5 [11.9-21.6]	14.3 [9.2-19.8]	18.3 [13.8-24.6]	21.8 [18.2-26.7] ¥
	Free wall TS,median,95%CI, %	18.0 [6.5-26.8]	11 [7.8-17.7]	12.5[8.6-18.5]	18.3 [9.3-21.8]
	BasalTS,median95%CI, %	28 [8.0-38.9]	11;0 [3.2-27.2]	11.5 [7.9-14.0]	9.0 [5.0-20.0]
	Mid TS, median 95%CI, %	15.0 [8.8-25.3]	12 [7.2-16]	12.0 [6.0-19.2]	17.0 [7.9-22.0]
	ApicalTS,median, 95%CI, %	12.5 [7-16.8]	12.0 [4.2-20.8]	15.0[8.0-26.0]	22.5 [14.9-28] ¥
	Septum TS, median 95%CI, %	16.2 [12.9-23.2]	13.7[4.9-22.0]	27.7[16.3-36.6]§	
	Strain rate, median 95%CI,s^{-1}	0.61 [0.49-0.76]	0.60 [0.39-0.65]	_	0.98 [0.93-1.13] ¥

Table 3: Comparison of standard echocardiographic parameters and peak systolic 2D strain of systemic ventricle function between d-TGA patients of group A and controls, and between d-TGA patients from group A and B. FAC: fractional area change, GLS: global longitudinal peak

systolic 2D strain, GTS: global transverse peak systolic 2D strain, LS: longitudinal peak systolic 2D strain, TS: transverse peak systolic 2D strain. TVI: time velocity integral, IVA: isovolemic acceleration, APSE: annular plane systolic excursion.*: significant difference between RV parameters of group A and group B, §: significant difference between RV parameters of group A and controls; ¥: significant difference between RV of group A and LV of controls. All p values were <0.05.

variables	Correlation coefficient r	95% confidence interval for r	p value
GLS	0.424	0.129-0.649	0.0065
GTS	-0.070	-0.970-0.243	0.7
dP/dT	0.047	0.389-0.307	0.8
Peak S wave	0.254	-0.055-0.518	0.3
CMR RVEF	0.214	-0.096-0.487	0.2
FAC	0.092	-0.218-0.385	0.6
Aortic VTI	0.260	-0.052-0.526	0.3
IVA	0.054	-0.254-0.353	0.7
TAPSE	0.264	-0.052-0.532	0.1
Tei	0.025	-0.288-0.334	0.9

Table 4: Correlation between standard echocardiographic and speckle tracking measurements of sRV function and percent predictive value of peak oxygen uptake. CMR RVEF: right ventricle ejection fraction by cardiac magnetic resonance imaging. FAC: fractional area change, GLS: global longitudinal peak systolic 2D strain, GTS: global transverse peak systolic 2D strain, VTI: velocity time integral, IVA: isovolumic acceleration, TAPSE: tricuspid annular plane systolic excursion.